METHODS FOR DISCOVERING AND SCORING SINGLE NUCLEOTIDE POLYMORPHISMS

Release Date: January 9, 1998

RFA: HG-98-001

P.T.

National Institutes of Health

Letter of Intent Receipt Date: March 25, 1998
Application Receipt Date: May 7, 1998

PURPOSE

The purpose of this Request for Applications (RFA) is to solicit applications for research grants to (1) develop genomic-scale technologies, or (2) implement pilot-scale or large-scale projects for the discovery and scoring of single nucleotide polymorphisms (SNPs). The pilot/large-scale projects may be for SNPs that are located throughout the genome or that are located in particular genome regions or in sets of genes related to particular processes, organs, or diseases.
The availability of a dense collection of SNPs will stimulate many areas of biological research, including the identification of the genetic components of disease.

HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This Request for Applications (RFA), "Methods for Discovering and Scoring Single Nucleotide Polymorphisms", is related to several priority areas, including cancer, heart disease and stroke, diabetes and chronic disability conditions, maternal and infant health, and others. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign for-profit and non-profit organizations, public and private organizations, such as universities, colleges, hospitals, laboratories, companies, units of State and local governments, and eligible agencies of the Federal Government. Applications from social/ethnic minority individuals, women, and persons with disabilities are encouraged.

MECHANISM OF SUPPORT

All of the institutes participating in this RFA will use the National Institutes of Health (NIH) individual research project grant (R01). In addition, several of the institutes will use the program project grant (P01) or the pilot project/feasibility study (R21) mechanisms; investigators considering applying for either an R21 or P01 grant should contact the appropriate program officer (see below). The total project period for R01 and P01 applications submitted in response to the present RFA may not exceed 3 years. The direct cost per year for R01 or P01 grants may not exceed $500,000 without prior discussion with the relevant program officer.

Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. Awards will be administered under PHS grants policy as stated in the Public Health Service Grants Policy Statement. Future unsolicited competing continuation applications will compete with all investigator-initiated applications and will be reviewed according to the customary peer review procedures.

All applications received in response to this solicitation will, for administrative reasons, be assigned initially to NHGRI. After discussions among the participating Institutes and Centers, applications will be reassigned to the Institute(s) or Center(s) that are programmatically most appropriate. Because the scope of the research proposed in response to this RFA encompasses the interests of several NIH Institutes and Centers, applications may receive dual assignments based on the established PHS referral guidelines. Awards will be made and managed by the NHGRI and/or the other participating Institutes and Centers. The earliest anticipated award date is September 30, 1998.

FUNDS AVAILABLE

It is anticipated that $10 million per year will be available for this initiative. Awards pursuant to this RFA are contingent upon the availability of funds for this purpose. The amount of funding for these projects may be increased if a large number of highly meritorious applications are received and if funds are available. Only applications that are found to be of high scientific merit will be

considered for funding and not all of the funds will be spent if there are not enough highly meritorious applications. Funding in future years will be subject to the availability of funds.

RESEARCH OBJECTIVES

Background

Genetic factors appear to contribute to virtually every human disease, conferring susceptibility or resistance, affecting the severity or progression of disease, and interacting with environmental influences. Much of current biomedical research, in both the public and private sectors, is based upon the expectation that understanding the genetic contribution to disease will revolutionize diagnosis, treatment, and prevention. Defining and understanding the role played by genetic factors in disease will also allow the non-genetic, environmental influence(s) on disease to be more clearly identified and understood.

Analysis of DNA sequence variation is becoming an increasingly important source of information for identifying the genes involved in both disease and in normal biological processes, such as development, aging, and reproduction. In trying to understand disease processes, information about genetic variation is critical for understanding how genes function or malfunction, and for understanding how genetic and functional variation are related. Response to therapies can also be affected by genetic differences. Information about DNA sequence variation will thus have a wide range of application in the analysis of disease and in the development of diagnostic, therapeutic, and preventative strategies.

Completion of the first human DNA sequence, through the efforts of the Human Genome Project (HGP), is expected by 2005. While this will be of immense significance for many reasons, the HGP will actually produce very little information about DNA sequence variation within the human population. Although the DNA sequence that will be produced by the HGP will come from several individuals, at most positions the sequence will come from only one. The exceptions will be regions where overlapping clones from different chromosomes will be sequenced, but such overlap will be less than 10% of the complete sequence. Even in the overlap regions, DNA from only two chromosomes will be represented at any given site. Thus, additional studies are needed to discover the amount and distribution of variation in human DNA.

There are several types of DNA sequence variation, including insertions and deletions, differences in the copy number of repeated sequences, and single base pair differences. The latter are the most frequent. They are termed single nucleotide polymorphisms (SNPs) when the

variant sequence type has a frequency of at least 1% in the population. SNPs have many properties that make them attractive to be the primary analytical reagent for the study of human sequence variation. In addition to their frequency, they are stable, having much lower mutation rates than do repeat sequences. Detection methods for SNPs are potentially more amenable to being automated and used for large-scale genetic analysis. Most importantly, the nucleotide sequence variations that are responsible for the functional changes of interest will often be SNPs.

As noted, SNPs are very common in human DNA. Any two random chromosomes differ at about 1 in 1000 bases. For any particular polymorphic base (i.e., a base where the least common variant has a frequency of at least 1% in the population), only half or fewer of random pairs of chromosome differ at that site. Thus, there are actually more sites that are polymorphic in the human population, viewed in its entirety, than the number of sites that differ between any particular pair of chromosomes. Altogether, there may be anywhere from 6 million to 30 million nucleotide positions in the genome at which variation can occur in the human population. Thus, overall, approximately one in every 100 to 500 bases in human DNA may be polymorphic.

Information about SNPs will be used in three ways in genetic analysis. First, SNPs can be used as genetic markers in mapping studies. SNPs can be used for whole-genome scans in pedigree-based linkage analysis of families. A map of about 2000 SNPs has the same analytical power for this purpose as a map of 800 microsatellite markers, currently the most frequently used type of marker. Second, when the genetics of a disease are studied in individuals in a population, rather than in families, the haplotype distributions and linkage disequilibria can be used to map genes by association methods. For this purpose, it has been estimated that 30,000 to as many as 300,000 mapped SNPs will be needed.

Third, genetic analysis can be used in case-control studies to directly identify functional SNPs contributing to a particular phenotype. Because only three to five percent of the human DNA sequence encodes proteins, most SNPs are located outside of coding sequences. But SNPs within protein-coding sequences (which have recently been termed cSNPs) are of particular interest because they are more likely than a random SNP to have functional significance. It is also undoubtedly the case that some of the SNPs in non-coding DNA will also have functional consequences, such as those in sequences that regulate gene expression. Discovery of SNPs that affect biological function will become increasingly important over the next several years, and will be greatly facilitated by the availability of a large collection of SNPs, from which candidates for polymorphisms with functional significance can be identified. Accordingly, discovery of a large number of SNPs in human DNA is one objective of this RFA.

SNPs will be particularly important for mapping and discovering the genes associated with common diseases. Many processes and diseases are caused or influenced by complex interactions among multiple genes and environmental factors. These include processes involved in development and aging, and common diseases such as diabetes, cancer, cardiovascular and pulmonary disease, neurological diseases, autoimmune diseases, psychiatric illnesses, alcoholism, common birth defects, and susceptibility to infectious diseases, teratogens, and environmental agents. Many of the alleles associated with health problems are likely to have low penetrance, meaning that only a few of the individuals carrying them will develop disease. However, because such polymorphisms are likely to be very common in the population, they make a significant contribution to the health burden of the population. Examples of common polymorphisms associated with an increased risk of disease include the ApoE4 allele and Alzheimer's disease, and the APC I1307K allele and colon cancer.

Most of the successes to date in identifying (a) the genes associated with diseases inherited in a Mendelian fashion, and (b) the genetic contribution to common diseases, e.g., BRCA1 and 2 for breast cancer, MODY 1, 2, and 3 for type 2 diabetes, and HNPCC for colon cancer, have been of genes with relatively rare, highly penetrant variant alleles. These genes are well-suited to discovery by linkage analysis and positional cloning techniques. However, the experimental techniques and strategies useful for finding the low penetrance, high frequency alleles involved in disease are usually not the same, and are not as well developed, as those that have been successfully applied in positional cloning. For example, pedigree analysis of families often does not have sufficient power to identify common, weakly contributing loci. The types of association studies that do have the power to identify such loci efficiently require new approaches, techniques, and scientific resources to make them as robust and powerful as positional cloning. Among the resources needed is a genetic map of much higher density than the existing, microsatellite-based map. Association studies using a dense map should allow the identification of disease alleles even for complex diseases. SNPs are well suited to be the basis of such a map.

Available technologies have been used to discover SNPs with a reasonable degree of success. Thus, there is an opportunity to begin to test the feasibility of applying these methods in a high throughput, large-scale fashion to discover large numbers of SNPs. At the same time, there is clearly a need to improve these methods and to develop new approaches to SNP discovery. Current methods for the discovery of SNPs are often not particularly appropriate to score known SNPs in genotyping assays, and the available scoring techniques leave much to be desired in terms of throughput, efficiency and cost. Thus, there is also a critical need to develop new methods for scoring known SNPs.

Technology development spans a spectrum of stages. Initially it involves the development of a new methodology or the significant improvement of an existing methodology to the point of proof of principle. The method must then be reduced to practice. For such a new method to have a significant impact on genomic studies, it must also be shown that it can be used efficiently on a large-scale or genomic basis; this requires another level of technology development. This RFA is intended to solicit applications that address any of these phases of technology development. Specifically, this RFA is intended to solicit research projects of two types: (1) development of new or improved methods, and (2) pilot-scale or large-scale projects, for SNP discovery and scoring. Of particular interest are technologies that can be applied at the "genomic scale" cost-efficiently, and can be easily exported into other laboratories, or in other ways made readily accessible to investigators.

Objectives and Scope

The tools needed to discover and score SNPs efficiently are just beginning to emerge and many more robust technologies are needed. The Human Genome Project has been successful in generating information and resources rapidly and economically, in part, by developing and applying high-throughput and efficient technologies. Therefore, the NIH seeks the development of technologies that can be applied in similar ways to the rapid and efficient discovery of SNPs and the scoring of SNPs in many samples. Large-scale projects for SNP discovery will allow comparison of the various existing technologies, particularly with respect to scalability, and will begin to generate a large collection of SNPs.

Applications are solicited in these areas:

1. Development of new or improved methods for high throughput, cost-efficient discovery or scoring (or both) of SNPs. SNP "discovery" involves finding new SNPs. SNP "scoring" involves methods to determine the genotypes of many individuals for particular SNPs that have already been discovered. Methods that involve "wet bench" approaches, computational approaches, or multiplexing are appropriate. Proposed methods may focus on obtaining SNPs throughout the genome, or may focus on cSNPs; they may also target particular types or sets of genes. Methods that yield additional information (e.g. map location, haplotypes) at the same time as the SNP itself are appropriate, although the costs and benefits of obtaining the additional information must be discussed. Applicants who propose to develop new methods for SNP discovery or scoring should discuss the potential advantages of the proposed methods over existing methods.

2. Pilot-scale or large-scale projects for SNP discovery, scoring, or both.

Pilot-scale or large-scale projects may be proposed that target random SNPs or cSNPs on a genome-wide basis, or all of the SNPs within a defined region of one to several megabases. Applications may focus on genes involved in particular processes or diseases of interest to particular Institutes, as listed below. Methods that focus on finding SNPs in coding sequences or regulatory regions, or on finding SNPs for functional variants of genes, are of particular interest. However, the methods must be capable of being applied on a large scale. Proposals should include a discussion of error rates, costs, and ease of scale up.

Most of the Institutes and Centers participating in this RFA have interests in genes that are related to particular processes, organs, or diseases, as listed below. In addition, some are interested in supporting development of methods that are either general or specific to genes in which they are interested, as noted below. Applications that propose to identify SNPs in or around genes of particular interest to a participating Institute are particularly welcome.

NCI - Genes involved in cancer.

NCRR - Genes and non-coding regions anywhere in the genome.

NEI - Genes involved in the development, function, and diseases of the eye.

NHGRI - Genes and non-coding regions anywhere in the genome.

NHLBI - Genes involved in the development, function, regulation, and diseases of the cardiovascular, pulmonary, and hematological systems.

NIA - Genes for repair enzymes for DNA, proteins, and lipids; antioxidant enzymes; apoptosis-related proteins; receptors; stress response proteins; transcription factors and neurodegenerative diseases of aging. Specific gene region: the WRN gene for Werner's syndrome.

NIAAA - Genes involved in function of the central nervous system, e.g., those encoding neurotransmitter receptors, transporters, and biosynthetic enzymes, neurotrophic factors and their receptors, ion channels, signal transducing proteins, and transcription factors. Genes whose products mediate the toxic effects of alcohol.

NIAID - Genes involved in susceptibility to infectious diseases, allergy, and autoimmunity.

NIAMS - Genes involved in arthritis and musculoskeletal and skin diseases.

NICHD - Genes involved in developmental biology, gametogenesis, fertilization, embryogenesis, organogenesis, and reproductive endocrinology; genes associated with the formation of birth defects; genes involved in mental retardation, autism and other developmental disabilities; genes associated with learning, behavior, and temperament; and genes affecting drug metabolizing enzymes in children.

NIDA - Genes involved in drug abuse and addiction.

NIDCD - Genes related to normal and disordered mechanisms of communication, including hearing, balance, voice, speech, language, taste and smell.

NIDDK - Genes involved in diabetes and digestive and kidney diseases.

NIDR - Genes involved in the development, function, and diseases of craniofacial, oral, and dental tissues.

NIEHS - Genes controlling the distribution and metabolism of toxicants; genes for DNA repair pathways; genes for the cell cycle control system; genes for cell death and differentiation; and genes for the signal transduction systems controlling expression of the genes in the other categories. For NIEHS, participation in this RFA is the first phase of the Environmental Genome Project; see http://dir.niehs.nih.gov/dirosd/policy/.

NIGMS - Genes and non-coding regions not targeted to disease.

NIMH - Genes involved in behavior, mental disorders, and the development, function, and regulation of the central nervous system.

NINDS - Genes involved in neurological processes, in particular those genes or chromosomal regions identified as related to neurological disorders or stroke.

The following Institutes and Centers are interested in supporting the development of methods that are either general or specific to genes in which they are interested - NCI, NCRR, NHGRI, NHLBI, NIA, NIAAA, NIAID, NIDA, NIDDK, NIDR, NIEHS, NIGMS, and NIMH.

Population Resources. Most genetic variation occurs within rather than between ethnic groups; this means that sequence variants that are common in one group are likely to be found in other groups as well. Efforts are currently under way to establish a central repository of anonymous

DNA samples as a resource for the discovery of SNPs. This resource may be available by the time applications are funded under this RFA. However, applicants should propose one or more alternative sources of appropriate samples in case the planned resource is not available by that time. Applicants for SNP discovery projects should provide plans that will allow the detection of SNPs that are common in the U.S. population. In most populations studied, the minimum frequency should be 1% for cSNPs and 10% for SNPs that are not in coding regions.

Human Subjects Issues Associated with SNP Discovery. Recently it has become evident that human subjects issues are raised by the large-scale sequencing of human genomic DNA because large amounts of DNA sequence information from single individuals will be generated. These issues are discussed in "Guidance on Human Subjects Issues in Large-Scale DNA Sequencing," which can be found on the NHGRI Home Page at http://www.NHGRI.nih.gov/Grant_info/Funding/Statements/large_scale.html. As a result of the research supported under this RFA, it is possible that an analogous situation might exist, i.e., that enough information might be developed about the genotypes of the individuals whose DNA was used to discover SNPs to allow them to be identified and, consequently, become subject to any risk(s) that might arise as a result of that identification. Applicants should address any special human subjects issues that arise as a result of their proposed research.

Data and Materials Dissemination. The sharing of materials, data, and software in a timely manner has been an essential element in the rapid progress that has been made in genome research. While Public Health Service (PHS) policy requires that investigators make unique research resources, including DNA sequences and mapping information, readily available when they have been published (PHS Grants Policy Statement, April 1, 1994, pp. 8-25 to 8-26), the advisors to the NIH and the Department of Energy (DOE) genome programs have encouraged more rapid sharing. This has, in fact, become the norm in the genome community.

NIH is interested in ensuring that the information about SNPs that is developed through this RFA becomes readily available to the research community for further research and development, in the expectation that this will eventually lead to products of benefit to the public. For this reason, NIH is concerned that patent applications on large numbers of SNPs, in the absence of such demonstrated utility, might have a chilling effect on the future development of products that can improve the public health. At the same time, NIH recognizes the rights of grantees to elect and retain title to subject inventions developed under Federal funding under the provisions of the Bayh-Dole Act. Indeed, for inventions developed in its intramural program, NIH does file patent applications, in accord with a set of policies that are described at http://www.nih.gov/od/ott/200po6.htm.

To address the joint interests of the government in the availability of, and access to, the results of publicly funded research and in the opportunity for economic development based on those results, NIH requires applicants who respond to this RFA to develop and propose specific plans for sharing the data, materials, and software generated through the grant. For this purpose, it is the opinion of the NIH that dissemination of such developments via individual laboratory web sites is not sufficient, as it would force interested investigators to have to search several different data collections to make use of the results of this initiative. It is preferable that data pertaining to all SNPs discovered or scored should be placed in a common, public database. Any additional information known, such as map location, should similarly be deposited in that database. A specific database suitable for this purpose will be identified when the awards are made.

The initial review group will comment on the proposed plan for sharing and data release. The adequacy of the plan will also be considered by NIH staff as one of the criteria for award. The proposed sharing plan, after negotiation with the applicant when necessary, will be made a condition of the award. Evaluation of renewal applications will include assessment of the effectiveness of data, material, and software release.

Applicants are also reminded that the grantee institution is required to disclose each subject invention to the Federal Agency providing research funds within two months after the inventor discloses it in writing to grantee institution personnel responsible for patent matters. The awarding Institute or Center reserves the right to monitor grantee activity in this area to ascertain if patents on large numbers of SNPs of ill-defined functionality are being filed.

Where appropriate, grantees may work with the private sector to make unique resources available to the larger biomedical research community at a reasonable cost. Applicants may request funds to defray the costs of sharing materials or submitting data, with adequate justification.

POST-AWARD MANAGEMENT

During the course of the grant period, it is anticipated that technologies will improve and the rate of progress and focus of work supported by the grant(s) may change. During the course of the award period, the principal investigators may be invited to meet with NIH program staff in Bethesda, MD, to review scientific progress. Other scientists external to and knowledgeable about these studies may also be invited to participate. Budget requests should include travel funds for the PI to meet annually in the Washington DC area, should such meetings be advisable.

INCLUSION OF WOMEN AND MINORITIES IN RESEARCH INVOLVING HUMAN SUBJECTS

It is the policy of the NIH that women and members of minority groups and their subpopulations must be included in all NIH supported biomedical and behavioral research projects involving human subjects, unless a clear and compelling rationale and justification is provided that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. This policy results from the NIH Revitalization Act of 1993 (Section 492B of Public Law 104-43).

All investigators proposing research involving human subjects should read the "NIH Guidelines for Inclusion of Women and Minorities as Subjects in Clinical Research," which have been published in the Federal Register of March 28, 1994 (FR 59 14508-14513), and in the NIH GUIDE FOR GRANTS AND CONTRACTS of March 18, 1994, Volume 23, Number 11.

Investigators may obtain copies from these sources or from program staff or contact person listed under INQUIRIES. Program staff may also provide additional relevant information concerning the policy.

LETTER OF INTENT

Prospective applicants are encouraged to discuss their research objectives and the appropriate grant mechanism with NIH staff in the relevant Institute or Center early in their planning process. Prospective applicants are asked to submit, by March 25, 1998, a letter of intent that includes a descriptive title of the proposed research, the name, address, email address, and telephone number of the principal investigator, the identities of other key personnel and participating institutions; and the number and title of this RFA. Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains will allow NIH staff to estimate the potential review workload and to avoid conflict of interest in the review.

The letter of intent is to be sent to:

Lisa D. Brooks, Ph.D.
Division of Extramural Research
National Human Genome Research Institute
Building 38A, Room 614, MSC 6050
Bethesda, MD 20892-6050
Telephone: (301) 496-7531

FAX: (301) 480-2770
Email: Lisa_Brooks@nih.gov

APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 5/95) is to be used in applying for these grants. Applications kits are available at most institutional offices of sponsored research and may be obtained from the Division of Extramural Outreach and Information Resources, National Institutes of Health, 6701 Rockledge Drive, MSC 7910, Bethesda, MD 20892-7910, telephone 301/435-0714, email: ASKNIH@od.nih.gov.

The RFA label available in the PHS 398 (rev. 5/95) application form must be affixed to the bottom of the face page of the application. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review. In addition, the RFA title and number must be typed on line 2 of the face page of the application form and the YES box must be marked.

Submit a signed, typewritten original of the application and three signed photocopies, in one package to:

CENTER FOR SCIENTIFIC REVIEW
NATIONAL INSTITUTES OF HEALTH
6701 ROCKLEDGE DRIVE, ROOM 1040 - MSC 7710
BETHESDA, MD 20892-7710
BETHESDA, MD 20817 (for express/courier service)

At the time of submission, two additional copies of the application, including appendices, must also be sent to:

Dr. Rudy Pozzatti
Office of Scientific Review
National Human Genome Research Institute
Building 38A, Room 613
38 Library Drive, MSC 6050
Bethesda, MD 20892-6050

Applications must be received by May 7, 1998. If an application is received after that date, it will be returned to the applicant without review. The Center for Scientific Review (CSR) will not accept any application in response to this RFA that is essentially the same as one currently pending initial review, unless the applicant withdraws the pending application. The CSR will also not accept any application that is essentially the same as one already reviewed. This does not preclude the submission of substantial revisions of applications already reviewed, but such applications must include an introduction addressing the previous critique. The applicants should also ensure that their revised applications respond to the review criteria by which the applications in response to this RFA will be evaluated.

REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed for completeness by CSR and for responsiveness to the RFA by NIH program staff. Incomplete applications will be returned to the applicant without further consideration. If the application is not responsive to the RFA, NIH staff will contact the applicant to determine whether to return the application to the applicant or submit it for review in competition with unsolicited applications at the next review cycle.

Those applications that are complete and responsive will be evaluated for scientific and technical merit in accordance with the criteria stated below by an appropriate peer review group convened by the NHGRI. As part of the initial merit review, all applications will receive a written critique and may undergo a process in which only those applications deemed to have the highest scientific merit will be discussed and assigned a priority score. All applications will receive a second level of review by the appropriate National Advisory Council.

Review criteria are:

o Significance: For technology development proposals, does this application address the development of a promising technology that can be usefully applied to the rapid and efficient discovery or scoring of SNPs? If the aims of the application are achieved, how will it improve the capabilities of researchers to discover SNPs or use SNPs in the genetic analysis of complex traits?

o For pilot-scale/large scale SNP discovery proposals, does this application address the efficient and rapid development of a useful resource of SNPs? If the aims of the application are achieved, how much will the SNP collection that is available to the research community be improved?

o Approach: Are the conceptual framework, design, methods, and analyses appropriate and adequate to accomplish the aims of the project? For pilot-scale/large-scale projects, are the methods adequate to allow the rapid, efficient detection of SNPs? Does the applicant acknowledge potential problem areas and consider alternate approaches? Is the scientific and technical merit of the proposed research sufficient to advance the objectives of the RFA?

o Innovation: Does the project employ novel concepts, approaches or method? Are the aims original and innovative? Does the project propose to develop new or significantly improved methodologies or technologies for SNP discovery or scoring?

o Investigator: Are the Principal Investigator and staff appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level of the principal investigator and other researchers (if any)?

o Scalability: For technology development or pilot-scale SNP production projects, what is the likelihood that the technology or approach will be able to be used efficiently at a full production level in a timely manner?

o Environment: Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed experiments take advantage of unique features of the scientific environment or employ useful collaborative arrangements? Is there evidence of institutional support?

o Budget and duration: Are the proposed budget and duration appropriate in relation to the proposed research?

The availability of special opportunities for furthering research programs through the use of unusual talent resources, populations, or environmental conditions in other countries which are not readily available in the United States or which provide augmentation of existing U.S. resources will be considered in the review.

The initial review group also will examine the provisions for the protection of human and animal subjects, and the safety of the research environment. For R21 applications, preliminary data are not required. However, the applicant does have the responsibility to develop a sound research plan and to present any other information that can be considered as evidence of feasibility.

The initial review group will also be asked to comment on the plans for making the data and materials developed under the proposed project accessible to the biomedical research community: Will the forthcoming methodologies, resources, software, and collections of SNPs be usable by, and accessible to, the broad scientific community of biomedical researchers who are discovering and using SNPs in a wide range of research investigations? Any opinions expressed by the reviewers about this aspect of the proposal will be recorded as an administrative note.

AWARD CRITERIA

The earliest anticipated date of award is September 30, 1998. Subject to the availability of funds, and consonant with the priorities of this RFA, the participating Institutes and Centers will provide funds for a project period of up to three years. Factors that will be used to make award decisions are:

- quality of the proposed project as determined by peer review;
- balance among the projects in addressing different experimental approaches and their complementarity to other ongoing efforts;
- adequacy of plans to make data and material developed as a result of the proposed research accessible to the biomedical research community in a timely manner; and
- availability of funds.

INQUIRIES

Written, telephone, and email inquiries concerning this RFA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues and mechanisms of support to the following NIH staff.

Lisa D. Brooks, Ph.D.
Division of Extramural Research
National Human Genome Research Institute
Building 38A, Room 614, MSC 6050
Bethesda, MD 20892-6050
Telephone: (301) 496-7531
FAX: (301) 480-2770
Email: Lisa_Brooks@nih.gov

Grace L. Shen, Ph.D.
Division of Cancer Biology
National Cancer Institute
6130 Executive Boulevard, Room 501
Rockville, MD 20892-7381
Telephone: (301) 496-5226
FAX: (301) 496-8656
Email: gs35r@nih.gov

Marjorie Tingle, Ph.D
Health Science Administrator
National Center for Research Resources
6705 Rockledge Drive, Room 6154
Bethesda, MD 20892
Telephone: (301) 435-0772
FAX: (301) 480-3659
Email: marjoriet@ep.ncrr.nih.gov

Maria Y. Giovanni, Ph.D
National Eye Institute
Executive Plaza South, Suite 350, MSC 7164
Bethesda, MD 20892-7164
Telephone: (301) 496-0484
FAX: (301) 402-0528
Email: myg@ nei.nih.gov

Stephen C. Mockrin, Ph.D.
Division of Heart and Vascular Diseases
National Heart, Lung, and Blood Institute
TWO Rockledge Centre
6701 Rockledge Drive, Suite 9044, MSC 7940
Bethesda, MD 20892-7940
Telephone: (301) 435-0477
FAX: (301) 480-1336
Email: mockrins@gwgate.nhlbi.nih.gov

Huber R. Warner, PhD

Biology of Aging Program
National Institute on Aging
Gateway Building, Room 2C231
Bethesda, MD 20892
Telephone: (301) 496-6402
FAX: (301) 402-0010
Email: warnerh@exmur.nia.nih.gov

Robert W.Karp, Ph.D.
National Institute on Alcohol Abuse and Alcoholism
Division of Basic Research
6000 Executive Boulevard, Suite 402, MSC 7003
Bethesda, MD 20892-7003
Telephone: (301) 443-4223
FAX: (301) 594-0673
Email: rkarp@willco.niaaa.nih.gov

Vicki Seyfert, Ph.D.
Division of Allergy, Immunology and Transplantation
National Institute of Allergy and Infectious Diseases
6003 Executive Boulevard, Room 4A21
Bethesda, MD 20852
Telephone: (301) 496-7551
FAX: (301) 402-2571
Email: vs62y@nih.gov

Steven J. Hausman, Ph.D.
Extramural Program
National Institute of Arthritis and Musculoskeletal and Skin Diseases
Building 45, Room 5AS-13F, MSC 6500
Bethesda, MD 20892-6500
Telephone: (301) 594-2463
FAX: (301) 480-4543
Email: sh41g@nih.gov

A. Tyl Hewitt, Ph.D.
Genetics and Teratology Branch

National Institute of Child Health and Human Development
Executive Building, Room 4B01
6100 Executive Blvd., MSC 7510
Bethesda, MD 20892
Telephone: (301) 496-5541
FAX: (301) 402-4083
Email: HewittT@hd01.nichd.nih.gov

Theresa Lee, Ph.D.
Division of Basic Research
National Institute on Drug Abuse
5600 Fishers Lane, Room 10A19
Rockville, MD 20857
Telephone: (301) 443-6300
FAX: (301) 594-6043
Email: tl37h@nih.gov

Catherine McKeon, Ph.D.
Metabolic Diseases and Gene Therapy Research Program
National Institute of Diabetes and Digestive and Kidney Diseases
Building 45, Room 5AN.18B
Bethesda, MD 20892-6600
Telephone: (301) 594-8810
FAX: (301) 480-3505
Email: Catherine_McKeon@nih.gov

Rochelle K. Small, Ph.D.
Division of Human Communication
National Institute on Deafness and Other Communication Disorders
6120 Executive Boulevard, Room 400C, MSC 7180
Bethesda, MD 20892-7180
Telephone: (301) 402-3464
FAX: (301) 402-6251
Email: rochelle_small@nih.gov

Linda Thomas, Ph.D.
Division of Extramural Research

National Institute of Dental Research
Building 45, Room 4AN-24J
Bethesda, MD 20892-6402
Telephone: (301) 594-2425
(301) 480-8318
Email: ThomasL@de45.nidr.nih.gov

Jose M. Velazquez, Ph.D.
Program Administrator
National Institute of Environmental Health Sciences
P.O.Box 12233
Research Triangle Park, NC 27709
Telephone: (919) 541-4998
FAX: (919) 541-2843
Email: Velazqu1@niehs.nih.gov

Irene Eckstrand, Ph.D.
Program Director
Developmental and Cellular Processes Branch
National Institute of General Medical Sciences
45 Center Drive, Room 2AS.25K
Bethesda, MD 20892-6200
(301) 594-0943
(301) 480-2228 (fax)
Email: irene_eckstrand@nih.gov

Steven O. Moldin, Ph.D.
Division of Basic and Clinical Neuroscience Research
National Institute of Mental Health
5600 Fishers Lane, Room 10C-26
Rockville, MD 20857
(301) 443-2037
(301) 443-9890
Email: smoldin@nih.gov

Judy Small, Ph.D.
Division of Fundamental Neurosciences and Developmental Disorders

National Institute of Neurological Disorders and Stroke
Federal Building, Room 8C04
Bethesda, MD 20892
Telephone: (301) 496-5821
FAX: (301) 402-0887
Email: js134h@nih.gov

Direct inquiries regarding fiscal matters to:

Ms. Jean Cahill
Grants Management Officer
National Human Genome Research Institute
Building 38A, Room 613, MSC 6050
Bethesda, MD 20892-6050
Telephone: (301) 402-0733
FAX: (301) 402-1951
Email: Jean_Cahill@nih.gov

AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.172. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

The PHS strongly encourages all grant and contract recipients to provide a smoke-free workplace and promote the non-use of all tobacco products. In addition, Public Law 103-227, the Pro-Children Act of 1994, prohibits smoking in certain facilities (or in some cases, any portion of a facility) in which regular or routine education, library, day care, health care or early childhood development services are provided to children. This is consistent with the PHS mission to protect and advance the physical and mental health of the American people.

Return to Volume Index
Return to NIH Guide Main Index